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Discussion

Dr Malcolm V. Brock *(Baltimore, Md).* The authors present an elegant study using a mouse model to investigate the structural mechanics and the dynamic interactions of the pulmonary and bronchial circulations during chronic inflammation of the lungs. Although the bronchial circulation is known to account for less than 5% of the blood supply and to provide nourishment to the central airways, very little is known about the structure of the bronchial microcirculation. So little is known, in fact, that there has not even been a demonstration of the existence of bronchial circulation in the mouse before this report.

The authors' mouse model has been well validated in some of their previous work and seems to provide a very reliable, reproducible inflammatory response in the lung, with resulting edema and atelectasis, and histologically there is a very distinct infiltrate that develops. The authors show that the mice clinically become generally lethargic, have trouble breathing, and the smooth appearance of their fur is altered. They further show that the functional consequence of this is noncompliant, stiff lungs. They then take a very innovative approach in using a casting technique, along with a 3-dimensional SEM, to visualize the actual structural connections between the bronchial and pulmonary microcirculations. The results are very clear, dramatic photographs showing what happens to these connections anatomically during a chronic inflammatory response.

I have three questions. First, the casting at 4 days does give us a sort of one-shot view of what happens to these connections. Have you looked at any other time points?

Dr Ravnic. With regard to the timeline, we actually evaluated lungs 2, 4, and 6 days after the induction of pulmonary inflammation. At each of these time points we used histologic examination, corrosion casting, and ventilator measurements. The peak of inflammation consistently occurred at 72 to 96 hours, and this was paralleled by alterations in pulmonary mechanics, as well as an increased flow via the bronchial circulation, as demonstrated by the casts.

Dr Brock. Would you tell us a little bit about the functional and clinical implications of some of this work for our patients, and especially in terms of redefining clinical parameters that we can use for pressure and flow relationships, for example, during a pulmonary embolism?

Dr Ravnic. Because the bronchial and pulmonary microcirculations are so interconnected, it is suggested that alterations in the pulmonary circulation would alter flow and pressure in the bronchial circulation. For example, in inflammatory cases, such as a pulmonary embolism or other types of infection, where the pulmonary circulation autoregulates itself, to minimize ventilation-perfusion mismatching, bronchial flow may be augmented to continue to deliver systemic oxygenated blood as well as inflammatory cells. If we could devise a way to probe the bronchial circulation and its pressure and flow characteristics under these conditions, we might find a correlation with the amount of inflammation taking place in the lung.

Dr Brock. Finally, angiogenesis is known to contribute in many instances in the sort of pathologic damage and repair situation that you see during inflammation. Did you investigate or see any evidence of neovasculature formation in your model, and what about its functional significance?

Dr Ravnic. Although neovascularization is certainly a feasible adaptation during increased perfusion, we have not yet specifically looked at angiogenesis. We have only been able to demonstrate that this functional increase in perfusion occurs during inflammation. However, we do plan to investigate the effects of angiogenesis in the future, as well as any other structural adaptations that might occur in the bronchial circulation.

Dr Stephen G. Swisher *(Houston, Tex).* Do you know what the underlying cause of these interconnections is? Could it be the alveolar macrophages, and have you looked at any models where the macrophages are depleted?

Dr Ravnic. We have not looked at any models of macrophage depletion. As far as other cells involved in inflammation, we have been studying the role of platelets in altering the structure of the systemic microvascular network. We have not yet studied the role of platelets or microphages in altering the structure of the pulmonary network.